

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of : *Velikyan et al.*

Application No. : 10/552,206

Filing Date : September 14,, 2006

Art Unit : 1618

Title : Method of Obtaining Gallium-68 and Use Thereof and Device for
Carrying Out Said Method

Docket No. : PZ0333

Mail Stop Appeal Brief–Patents

Commissioner for Patents

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APPEAL BRIEF

Table of Contents

	<u>Page</u>
I. Real Party In Interest	3
II. Related Appeals and Interferences.....	3
III. Status of Claims	3
IV. Status of Amendments	3
V. Summary of Claimed Subject Matter	3
VI. Grounds Of Rejection To Be Reviewed On Appeal	4
VII. Argument	4
The Examiner's Rejection of Claims 1-19 Should be Reversed Since, Griffiths in view of Bottcher and in further view of Maier-Borst Fails to Disclose, Teach or Suggest All the Elements of Claims 1-19.....	5
VIII. Claims Appendix	10
IX. Evidence Appendix.....	12
X..... Related Proceedings Appendix.....	13

I. REAL PARTY IN INTEREST

The real party in interest in this Appeal is GE Healthcare, Inc., a part of General Electric ("GE").

II. RELATED APPEALS AND INTERFERENCES

There are no other appeals or interferences related to the instant appeal.

III. STATUS OF CLAIMS

Claims 1-19 are pending in this application. The Examiner has rejected all of these claims. Claims 1-19 as amended during prosecution are reproduced in the **Claims Appendix** attached hereto. Appellants are appealing the rejection of Claims 1-19.

IV. STATUS OF AMENDMENTS

A final Office Action was mailed on February 12, 2009. No claims have been amended thereafter.

V. SUMMARY OF CLAIMED SUBJECT MATTER

Independent Claim 1 describes a method of obtaining ^{68}Ga by contacting the eluate from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator with an anion exchanger comprising HCO_3^- as counterions and eluting ^{68}Ga from said anion exchanger.

Support for this claim can be found on page 3, line 24 to line 26 of the specification.

Independent claim 15 describes a kit for the preparation of ^{68}Ga from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator, which comprises a generator column and a second column that comprises an anion exchanger comprising HCO_3^- as counterions.

Support for this claim can be found on page 8, line 14 to line 16 of the specification.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues for review in this appeal arise from an Office Action dated February 12, 2009. The Examiner rejected claims 1-19 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Griffiths et al., WO03/059397A2 (“Griffiths”) in view of Bottcher et al., US 5,439,863 (“Bottcher”) and further in view of Maier-Borst et al., GB2056471A (“Maier-Borst”). Therefore, the issue in this appeal is:

1. Whether Griffiths in view of Bottcher and in further view of Maier-Borst disclose, teach, or suggest all the elements of claims 1-19?

VII. ARGUMENT

The Examiner rejected Claims 1-19 under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Griffiths et al., WO03/059397A2 (“Griffiths”) in view of Bottcher et al., US 5,439,863 (“Bottcher”) and further in view of Maier-Borst et al., GB2056471A (“Maier-Borst”).

Appellants respectfully request that The Board of Patent Appeals and Interferences (“Board”) should reverse the Examiner’s rejection for the reasons set forth below.

A. The Examiner's Rejection of Claims 1-19 Should be Reversed Since Griffiths in view of Bottcher and in further view of Maier-Borst Fails to Disclose, Teach or Suggest All the Elements of Claims 1-19.

The Examiner's Rejections of Claims 1-19 should be reversed since Griffiths in view of Bottcher and in further view of Maier-Borst fails to disclose, teach, or suggest all the elements of claims 1-19.

First, unlike the present invention, Griffiths does not disclose the preparation of the agents via microwave acceleration. Nor does Griffiths disclose an anion exchanger comprising quaternary amine functional groups, polystyrene-divinylbenzene and HCO_3^- as counterions.

Additionally, the objective of Bottcher is aimed at a process of preparing a neutral metal complex salt with additional coordinated ligands comprising reacting a complex-forming metal salt with a chelating ligand and a Lewis base in water and the optional presence of a solubilizer and an inorganic auxiliary base which forms a soluble salt an acid radical of the metal salt. Bottcher does not use the microwave activation technique disclosed in the present invention to carry out the coordination chemistry. Bottcher merely mentions in passing that the input of energy can also take place through the effect of ultrasound, microwaves, or a laser beam. Col. 3, lines 44-45. In other words, Bottcher does not elaborate or even further discuss any of these possible inputs of energy.

Even assuming, *arguendo*, that Griffiths in view of Bottcher are properly combinable, any such combination would completely teach away from the present invention. As noted by the

Federal Circuit:

A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

Para-Ordnance Mfg. v. SGS Importers Int'l, 73 F.3d 1085 (Fed. Cir. 1995).

Applicants respectfully submit that it is clear that Bottcher does not deem these inputs of energy as important parts of its patent. Bottcher presents using three separate inputs of energy on merely two lines throughout its entire patent. Furthermore, Bottcher does not teach that microwaves are preferred over using ultrasound or laser beams as inputs of energy. Bottcher does not disclose, teach, or suggest using a microwave oven as disclosed in the present invention to enhance or improve efficiency and reproducibility of the neutral metal complex salt formation. If Bottcher used the same microwave technology, such as a microwave oven, utilized in the present invention then Bottcher would have found that the use of microwave activation substantially improves the efficiency and reproducibility of its neutral metal complex salt formation.

Furthermore, even if assuming Griffiths in view of Bottcher are properly combinable, the references still have to be combinable with Maier-Borst.

The aim of the work by Maier-Borst was to synthesize an anion exchange resin for the separation of gallium-68 from germanium-68 avoiding the use of EDTA for elution as it was done before 1980s. Its aim does not collide with the claims 1-19 and the comparison is not relevant. In the instant invention, gallium-68 is eluted from a commercial generator already in ionic form. In particular the claims 1-19 consider: i) The preconcentration of gallium-68 which is needed for the efficiency of the labeling complexing reaction. Namely, the specific radioactivity for the chelator conjugated peptide labeling was increased 200-fold. ii) The volume was decreased 30 – fold, namely, from 6 mL to 200 μ L. This makes 30 – fold increase in peptide or any other macromolecule concentration. iii) The chelating ^{68}Ga -labeling reactions are sensitive to the presence of competing metal ions therefore it is important to purify the $^{68}\text{Ge}/^{68}\text{Ga}$ generator eluate from those elements. The ability of metal ions to form complexes with hydrochloric acid differs. The adsorbability of the negatively charged complexes of metals differs as well. Taking into account that the preconcentration procedure is based on the gallium ion ability to form GaCl_4^- complex, gallium can be purified from the competing metal ions using the anion-exchanging column.

Additionally, on page 3 of the Office Action dated February 12, 2009, the Examiner states in part that "...the assertion that Bottcher et al. does not deem microwave as an important part of its patent is merely the opinion of the applicant." Appellants respectfully disagree. Bottcher does not teach that microwaves are preferred over using ultrasound or laser beams as inputs of energy. Bottcher only mentions in passing that the input of energy can also take place through the effect of ultrasound, microwaves, or a laser beam. Col. 3, lines 44-45. Appellants wish to point out that "the prior art itself must provide a motivation or reason for the worker in

the art, without the benefit of the Applicant's specification, to make necessary changes in the reference device". See, *Ex parte Chicago Rawhide Manufacturing Co.*, 226 U.S.P.Q. 438 (PTO Bd. App. 1984). Additionally, it is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). (emphasis added).

It is therefore respectfully submitted that the 35 U.S.C. 103(a) rejections of claims 1-19 as being unpatentable over Griffiths in view of Bottcher in further view of Maier-Borst be withdrawn.

DOUBLE PATENTING

Claims 8-12 and 14 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1, 3-7, 11, 13, 15 of co-pending Application No. 10/552,134. In response, Applicants submit that claims will be amended or cancelled if the instant application is indicated to be allowable.

Further, claims 1, 2 6-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of copending Application No. 11/358,681. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated to allowable.

Still further, claims 1-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/552,134. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated to allowable.

CONCLUSION

In view of the foregoing, Appellants respectfully request that the Board reverse the rejections of Claims 1-19 as set forth in the Office Action mailed February 12, 2009, that the Board allow the pending claims since they are in condition for allowance, and that the Board grant any other relief as it deems proper.

Dated: July 13, 2009

Respectfully submitted,

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VIII. CLAIMS APPENDIX

1. Method of obtaining ^{68}Ga by contacting the eluate from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator with an anion exchanger comprising HCO_3^- as counterions and eluting ^{68}Ga from said anion exchanger.
2. Method according to claim 1 wherein the $^{68}\text{Ge}/^{68}\text{Ga}$ generator comprises a column comprising titanium dioxide.
3. Method according to claim 1 wherein 0.05 to 5 M HCl is used to elute ^{68}Ga from the $^{68}\text{Ge}/^{68}\text{Ga}$ generator.
4. Method according to claim 2 wherein 0.05 to 0.1 M HCl is used to elute ^{68}Ga from the $^{68}\text{Ge}/^{68}\text{Ga}$ generator.
5. Method according to claim 1 wherein water is used to elute ^{68}Ga from the anion exchanger.
6. Method according to claim 1 wherein the anion exchanger is a anion exchanger comprising quaternary amine functional groups.
7. Method according to claim 1 wherein the anion exchanger is a anion exchange resin based on polystyrene-divinylbenzene.
8. Method of producing a ^{68}Ga -radiolabelled complex by reacting ^{68}Ga obtained by the method according to claim 1 with a chelating agent.
9. Method according to claim 8 wherein the chelating agent is a macrocyclic chelating agent.
10. Method according to claim 8 wherein the chelating agent comprises hard donor atoms, preferably O and N.
11. Method according to claim 8 wherein the chelating agent is a bifunctional chelating agent

12. Method according to claim 11 wherein the chelating agent is a bifunctional chelating agent comprising a targeting vector selected from the group consisting of proteins, glycoproteins, lipoproteins, polypeptides, glycopolypeptides, lipopolypeptides, peptides, glycopeptides, lipopeptides, carbohydrates, nucleic acids, oligonucleotides or a part, a fragment, a derivative or a complex of the aforesaid compounds and small organic molecules.
13. Method according to claim 8 wherein the reaction is carried out using microwave activation.
14. Method according to claim 8 for the production of ^{68}Ga -radiolabelled PET tracers.
15. Kit for the preparation of ^{68}Ga from a $^{68}\text{Ge}/^{68}\text{Ga}$ generator, which comprises a generator column and a second column that comprises an anion exchanger comprising HCO_3^- as counterions.
16. Kit according to claim 15 further comprising means to couple the columns in series.
17. Kit according to claim 15 further comprising aqueous HCl to elute the ^{68}Ga from the generator column and/or water to elute the ^{68}Ga from the anion exchanger column, preferably, the HCl and the water being aseptically and in a hermetically sealed container.
18. Kit according to claim 15 further comprising a chelating agent, preferably a bifunctional chelating agent.
19. A method of using a kit according to claim 18 for the production of ^{68}Ga -radiolabelled PET tracers, comprising producing a ^{68}Ga -radiolabelled complex by reacting ^{68}Ga obtained by the method according to claim 1 with the chelating agent.

IX. EVIDENCE APPENDIX

Appellants hereby present the following publications/patents:

WO03/059397A2 (Griffiths et al.);

US 5,439,863 (Bottcher); and

GB2056471A (Maier-Bost).

This is the evidence relied upon by the Examiner for rejection of appealed Claims 1-19 in the final Office Action dated February 12, 2009.

X. RELATED PROCEEDINGS APPENDIX

There are no other appeals or interferences related to the instant appeal